

# Keeping Up the Pace

## Atrial Fibrillation in Clinical Practice

**Atrial fibrillation (AF) is the commonest arrhythmia in clinical practice. There are many therapeutic approaches, each one suited to a particular type of AF or to the patient being treated.**



By Indranill Basu Ray, MBBS, MD, DNB

### Bill's case

Bill, 52, presents with a five-year history of atrial fibrillation (AF). He had been seen by a cardiologist in the past and was started on sotalol, 80 mg, twice daily. He complained of severe fatigue and stopped the drug after having taken it for two years.

An angiogram was done as part of the workup by the cardiologist and the patient's coronaries were found to be normal. He also had an echocardiography (ECHO) done which showed no evidence of structural heart disease. He was referred to the arrhythmia clinic for further treatment.

When the patient was seen at the arrhythmia clinic, he was found to be totally asymptomatic. He had normal exercise tolerance and no cardiac risk factors were present. An ECG done at the clinic showed AF, with heart rate varying between 45 beats per minute (bpm) and 100 bpm.

The only medication he is currently taking is one daily tablet of acetylsalicylic acid.

**What would your prescription be?**

**For more on Bill, see page 40.**

### In this article:

- 1. When should atrial fibrillation be suspected?**
- 2. What drugs can be used for treatment?**
- 3. What are the interventional strategies?**

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**A**trial fibrillation (AF) is the most common arrhythmia encountered in clinical practice. Approximately 0.4% of people in the general population have permanent or intermittent AF and the prevalence increases to 6% in persons older than 80.<sup>1</sup> AF can result in serious complications, including congestive heart failure (CHF), myocardial infarction (MI), and thromboembolism.

Despite breakthroughs in drug management strategies, recurrence of AF is common; up to 50% of patients experience a relapse of AF within one year while taking antiarrhythmic drug therapy.<sup>2</sup> In fact, almost 20% of patients do not even tolerate effective drugs.<sup>3</sup> The limitations of pharmacologic therapy have led to novel nonpharmacologic, interventional approaches for the treatment of AF. This article reviews various therapeutic approaches.

### When should AF be suspected?

The diagnosis of AF should be considered in patients who present with complaints of shortness of breath, dizziness, or palpitations, as well as in patients with acute fatigue or exacerbation of CHF. In some patients, AF may be identified on the basis of an irregularly irregular pulse.

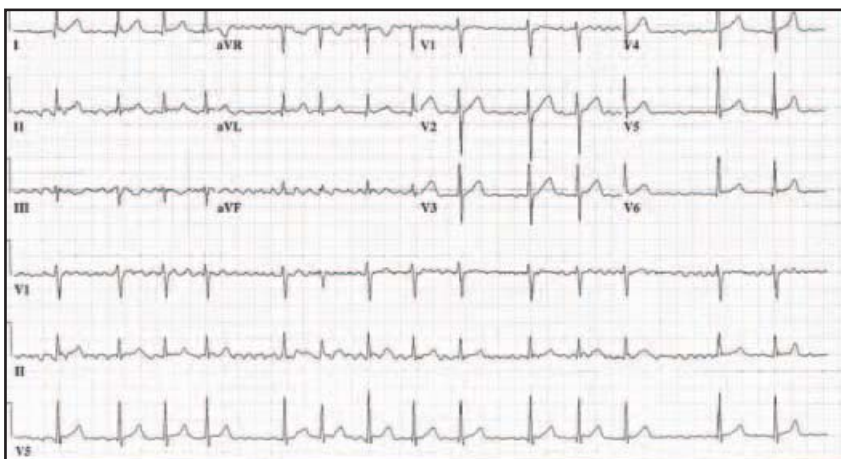


Figure 1. ECG showing atrial fibrillation.

Some cardiac conditions commonly associated with the development of AF include rheumatic mitral valve disease, coronary artery disease, CHF, and hypertension. Noncardiac conditions that can predispose patients to develop AF include hyperthyroidism, hypoxia, alcohol intoxication, and surgery.

The electrocardiogram (ECG) is the mainstay for diagnosis of AF. An irregularly irregular rhythm, inconsistent R-R interval, and the absence of P waves are usually noted on the ECG. AF waves (F waves), which are small, irregular waves seen as a rapid-cycle baseline fluctuation, indicate rapid atrial activity and are the hallmark of AF (Figure 1). AF should also be distinguished from atrial tachycardia, in which the atrial rate is regular, but conduction to the ventricles may be regular or irregular.

### What is the emergency management protocol?

There are three main goals in the treatment of AF: hemodynamic stabilization, ventricular rate control, and prevention of embolic complications. When AF does not terminate spontaneously, the ventricular rate should be treated to slow ventricular response and, if appropriate, efforts should be made to terminate AF and

restore sinus rhythm. The algorithm to follow is depicted in Figure 2.

Beta blockers and calcium channel blockers are the drugs of choice because they are effective in reducing the heart rate at rest and during exercise in patients with AF.

The calcium channel blockers diltiazem and verapamil are effective

## Algorithm for acute AF management

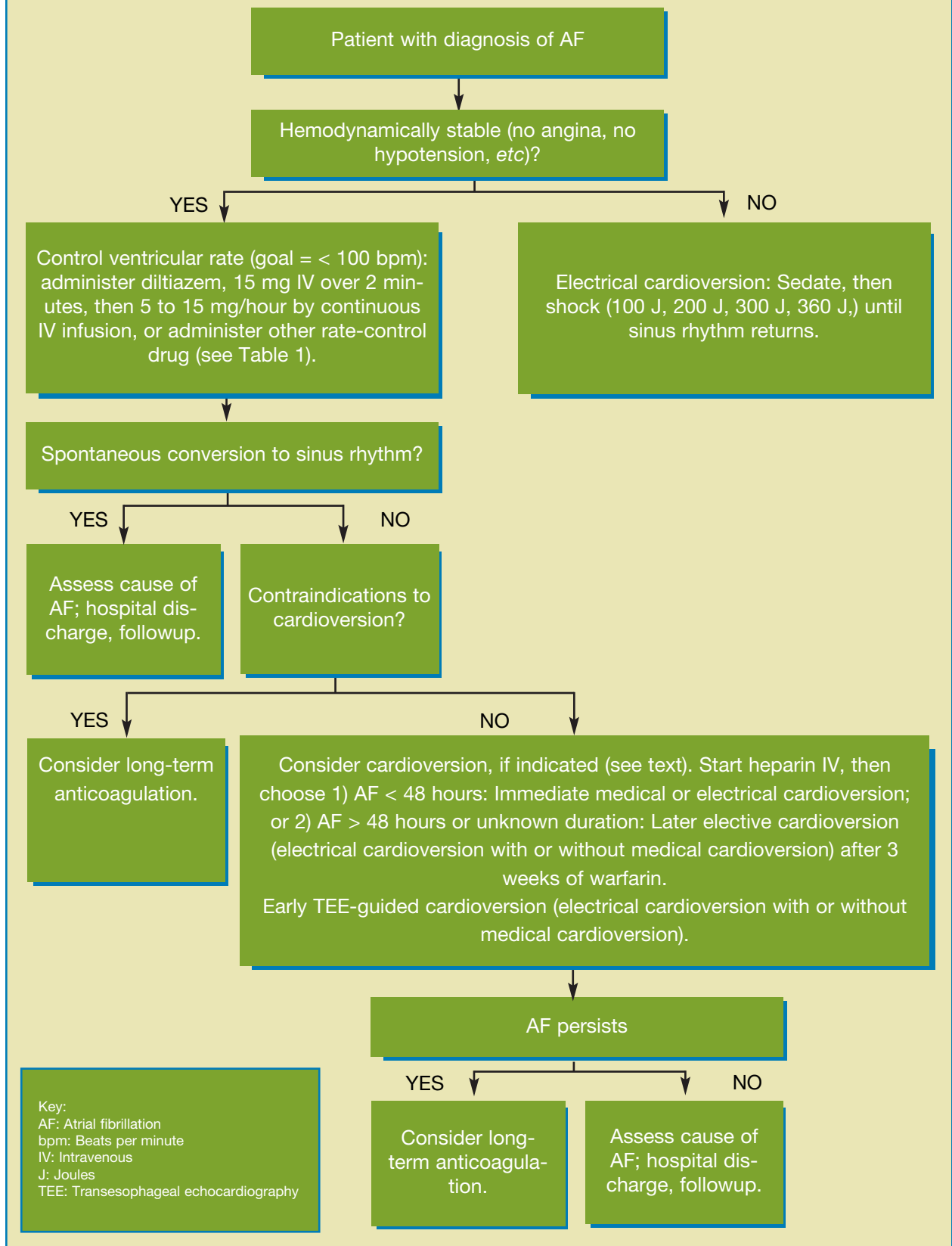


Figure 2. Algorithm for acute AF management.

for initial ventricular rate control in patients with AF. Other calcium channel blockers do not show antiarrhythmic effect and are not used. Verapamil can also be used for initial rate control, but should be used with particular caution because of the possibility of prolonged hypotension.

Beta blockers, such as propranolol and esmolol, may be preferable to calcium channel blockers in patients with MI or angina, but they should not be used in patients with asthma.

A concern with calcium channel blockers and beta blockers when used for initial ventricular rate control is their cardiodepressive effects, particularly in patients with CHF. However, as a common practice, one should feel comfortable in using these agents in patients with an ejection fraction > 20%.

Compared to beta blockers and calcium channel blockers, digoxin is less effective for ventricular rate control, particularly during exercise. Digoxin is most often used as adjunctive therapy because of its slower onset of action and its weak potency as an atrioventricular node-blocking agent.

There is evidence that combination regimens provide better rate control than any agent alone<sup>1</sup> (Table 1).

## Rate or rhythm control?

Hemodynamically unstable AF (e.g., with angina and/or hypotension) requires electrical cardioversion to be terminated. Following cardioversion, these patients may be put on antiarrhythmics to maintain sinus rhythm. Sotalol, amiodarone, and dofetilide all have moderate efficacy in maintaining sinus rhythm, with amiodarone appearing to be the most effective (Tables 2 and 3). Amiodarone and dofetilide have

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## **LIPITOR**\*: *Hitting targets.*

**EFFICACY** ➤ †A powerful demonstrated effect across key lipid parameters<sup>1</sup>



**LIPITOR is an HMG-CoA reductase inhibitor (statin).** LIPITOR is indicated as an adjunct to lifestyle changes, including diet, for the reduction of elevated total cholesterol, LDL-C, TG and apolipoprotein B in hyperlipidemic and dyslipidemic conditions (including primary hypercholesterolemia, combined [mixed] hyperlipidemia, dysbetalipoproteinemia, hypertriglyceridemia and familial hypercholesterolemia) when response to diet and other non-pharmacological measures alone has been inadequate.

LIPITOR also raises HDL-cholesterol and therefore lowers the LDL-C/HDL-C and Total-C/HDL-C ratios (Fredrickson Type IIa and IIb). These changes in HDL-C with HMG-CoA reductase inhibitors should be considered as modest when compared to those observed in LDL-C and do not play a primary role in the lowering of LDL-C/HDL-C and Total-C/HDL-C ratios.

See Prescribing Information for complete warnings, precautions, dosing and administration.

LIPITOR is contraindicated: During pregnancy and lactation; active liver disease or unexplained persistent elevations of serum transaminases exceeding 3 times the upper limit of normal; hypersensitivity to any component of this medication.

**Table 1**

## Drugs used for rate control

Drug	Initial dose	Maintenance dose	Notes
Diltiazem	15-20 mg IV over 2 min.; may repeat in 15 min.	5-15 mg/hr. by continuous IV	Convenient, easy to titrate to HR goal
Verapamil	5-10 mg IV over 2 min.; may repeat in 30 min.	Not standardised	More myocardial depression and hypotension than diltiazem
Esmolol	Bolus of 500 mcg/kg over 1 min.; may repeat in 5 min.	50-300 mcg/kg/min. by continuous IV	Very short-acting, easy to titrate to HR goal
Propranolol	1 mg IV over 2 mins.; may repeat every 5 min. to max. of 5 mg	1-3 mg IV every hr.	Short duration of action so need repeat dosing
Digoxin	0.25-0.5 mg IV; then 0.25 mg IV every 4-6 hr. to max. of 1 mg	0.125-0.25 mg/day IV or orally	Adjunct therapy; less effective for rate control than beta blockers or calcium channel blockers

IV: Intravenous  
HR: Heart rate

**Table 2**

## Dose and side effects of drugs used in maintaining sinus rhythm in AF

Drug	Daily dose	Adverse side effects
Amiodarone	100-400 mg/day	Photosensitivity, thyrotoxicity, pulmonary toxicity hepatic dysfunction, intestinal upset, bradycardia, insomnia, Torsade de pointes (rare)
Sotalol	240-320 mg/day	Torsade de pontes, CHF, bradycardia, exacerbation of COPD
Dofetilide	500-1,000 mcg	Torsade de pointes

CHF: Congestive heart failure  
COPD: Chronic obstructive pulmonary disease

The process of restoration of sinus rhythm for patients presenting to the emergency department with hemodynamically stable AF is decided based on many factors. In young patients (under 65 years old) with a single episode of AF,

been proven safe in patients with left ventricular dysfunction after MI and those with CHF. It is important to note that amiodarone exhibits minimum toxicity when given at a dose  $\leq$  400 mg/day and efforts should be made to keep patients requiring long-term therapy with this toxic drug at a dosage  $<$  400 mg. In clinical practice, amiodarone therapy can be started on an outpatient basis. However, with sotalol and dofetilide, it is preferable to start treatment in hospital with close monitoring for QT prolongation and any resultant Torsade de pointes.

but with structurally normal heart and no other risk factors for stroke, it is prudent to convert to sinus rhythm with rhythm control to avoid anticoagulation. Those with recurrent paroxysmal or chronic AF, but no risk factors for stroke are still not candidates for anticoagulants, as the risk of stroke without anticoagulants is equal to the risk of dangerous hemorrhagic bleeding with these drugs. Since there is no clear evidence that anticoagulants are beneficial to this patient group, the use of anticoagulants is not advocated in these individuals.

Factors that significantly increase the risk for stroke include previous stroke, previous transient ischemic attack or systemic embolus, hypertension, poor left ventricular systolic function, age greater than 75 years, prosthetic heart valve, and history of rheumatic mitral valve disease. Patients with one or more of these risk factors must be anticoagulated. Any aggressive efforts to maintain sinus rhythm is unwarranted and rate control is preferred.

The lowest risk for stroke is in patients with AF who are under 65 years old and have no history of cardiovascular disease, diabetes, or hypertension. However, if patients under 65 present with one or more of the aforementioned risk factors, they must also be treated with anticoagulants.

Efforts at restoring sinus rhythm are only advocated in high-risk patients if they do not tolerate or are contraindicated to rate-controlling medications, or if they remain symptomatic despite adequate antidromotropic medications.

## How can sinus rhythm be restored?

In hemodynamically unstable patients or in stable patients requiring cardioversion, the choice is between medical and electrical procedures.

### *Electrical cardioversion*

When patients with AF are hemodynamically unstable and are not responding to resuscitative measures, emergency electrical cardioversion is indicated; however, intravenous heparin must be given before the procedure. In stable patients, elective cardioversion may be performed after three weeks of warfarin therapy. To prevent thrombus formation warfarin should be continued for four weeks after cardioversion. Although the success rate for electrical cardioversion is high (90%), proper equipment and expertise are necessary for safe performance.<sup>4</sup> Also, sedation should be achieved before cardioversion is attempted and biphasic shocks are the pre-

## **LIPITOR**: Hitting targets.

**EFFICACY** ➤ †A powerful demonstrated effect across key lipid parameters<sup>1</sup>

**EXPERIENCE** ➤ More than ~~44~~ **48** million patient-years of experience<sup>2‡</sup>



Lipid levels should be monitored periodically and, if necessary, the dose of LIPITOR adjusted based on target lipid levels recommended by guidelines. Caution should be exercised in severely hypercholesterolemic patients who are also renally impaired, elderly, or are concomitantly being administered digoxin or CYP 3A4 inhibitors.

Liver function tests should be performed before the initiation of treatment, and periodically thereafter. Special attention should be paid to patients who develop elevated serum transaminase levels, and in these patients, measurements should be repeated promptly and then performed more frequently.

The effects of atorvastatin-induced changes in lipoprotein levels, including reduction of serum cholesterol on cardiovascular morbidity, mortality, or total mortality have not been established.

‡ A patient-year represents the total time of exposure to LIPITOR as defined by the sum of each patient time on LIPITOR.<sup>5</sup>

Table 3

### Drugs used in medical cardioversion of atrial fibrillation

Drug	Intravenous	Oral	Adverse effects
Amioarone	5 to 7 mg/Kg over 30 to 60 min., then 1.2-1,8 g/day continuous IV up to 10 g in divided doses. Maintenance of 200-400 mg/day	Inpatients: 1.2-1.8 mg/day up to 10 g in divided doses. Maintenance of 200-400 mg/day. Outpatients: 600 mg-800 mg/day up to 10 g in divided doses. Maintenance of 200-400mg/day	Hypertension, bradycardia, QT prolongation, Torsade de pointes, phlebitis (when given intravenously)
Dofetilide		The dose is based on creatine clearance: 60 mL/min.: 500 mcg bid 40-60 mL/min.: 250 mcg bid 20-40 mL/min.: 125 mcg bid > 20 mL/min.: contraindicated	QT prolongation, Torsade de pointes
Flecainide		200-300 mg	Hypotension, rapidly-conducting atrial flutter
Ibutilide	1 mg given slowly by IV over 10 min. Repeat 1 mg if required		QT prolongation, Torsade de pointes
Propafenone		450-600 mg	Hypotension, rapidly-conducting atrial flutter
Quinidine	1.5- 2 mg/kg given over 10-20 min.	0.75-1.5 g in divided doses	QT prolongation, Torsade de pointes

IV: Intravenous  
bid: twice daily

ferred strategy, as significantly fewer shocks are required for success.<sup>5</sup>

### Medical Cardioversion

Medical cardioversion may be appropriate when adequate facilities and support for

electrical cardioversion are not available or when patients have never been in AF before. It is also most effective when initiated within seven days of AF onset. Pharmacologic agents are effective in converting AF to sinus rhythm in about 40% of treated patients.<sup>4</sup>

## A followup on Bill

Since Bill has a history of AF and he is asymptomatic, chances are that he is in chronic AF. However, when we see him, despite being in AF, he has controlled ventricular rate not exceeding 100 bpm. This is unusual and indicates that he has underlying atrioventricular (AV) nodal disease. Thus, this young patient with no risk factors for stroke and with controlled ventricular rate, needs neither therapy with rate controlling agents nor anticoagulants. Because of the long history of AF and the fact that he is totally asymptomatic, cardioversion would not serve him well either.

His AV nodal disease would certainly worsen with time and lead him to need a pacemaker in the future. Because of this, the only advice we can give him is to be followed regularly by his physician for evidence of worsening conduction disorder.

### Take-home message

- AF should be considered in patients with irregularly irregular pulse who present with complaints of shortness of breath, dizziness, or palpitations, as well as in patients with acute fatigue or exacerbation of CHF.
- There are three main goals in the emergency treatment of AF: hemodynamic stabilisation, ventricular rate control, and prevention of embolic complications.
- In patients requiring cardioversion, the cardioversion must be preceded by anticoagulation therapy.
- Some interventional treatment strategies include nodal ablation or modification, catheter ablation, pacing, an atrial defibrillator, and surgical Maze procedure.
- Combination therapy is usually necessary for optimal care.

Medical cardioversion should be used only after careful consideration of the possibility of proarrhythmic complications, particularly in patients with structural heart disease or CHF. The anticoagulation protocol to be followed is identical to that followed during electrical cardioversion. Flecainide, ibutilide, and dofetilide are the most efficacious agents for medical conversion of AF, but propafenone and quinidine are also effective. Some investigators consider amiodarone to be the most effective agent for converting to sinus rhythm in patients who do not respond to other agents.

Cardioversion must be preceded by three to four weeks of anticoagulation to rule out intracardiac clots. If present, clots can move into circulation, producing cerebrovascular insufficiency and ischemic stroke. Most AF-derived strokes occur within the first 72 hours after medical or electrical cardioversion.<sup>6</sup>

## What are the indicators for intervention?

Interventional strategies are indicated in the following circumstances:

- symptomatic AF in patients not adequately controlled despite maximum tolerated drug therapy;
- patients not tolerating anticoagulants; and
- patients with AF who are not tolerating, or do not desire, long-term antiarrhythmics.

## What are the treatment options?

### *Nodal ablation versus modification*

The goal of atrioventricular (AV) nodal ablation and AV nodal modification is to obtain adequate ventricular rate control during AF which is refractory to drugs. The end point of the AV nodal ablation is to induce complete AV block with subsequent pacemaker implantation. The end point of the AV nodal modification is to achieve an average ventricular rate > 120 beats per minute during isoproterenol or atropine infusion.

AV nodal ablation and modification are not curative techniques. AF may remain and the embolic risk may not be reduced.

### *Catheter ablation*

Radiofrequency catheter ablation primarily aims to remove the foci that generate the arrhythmia. The mode of therapy in an individual patient depends on the pathophysiology of the arrhythmia.

The drawing of linear ablation lines in one or both the atria is among the various techniques available. The other technique which has shown impressive results is the electrical isolation of the pulmonary veins.<sup>7</sup>

## Pacing


Experience using pacemakers has shown that compared to patients who receive ventricular pacing only, patients who require pacing for bradyarrhythmias are less likely to develop AF if they are paced atrially as well as ventricularly. The above theory has been applied to test pacing treatment for the purpose of reducing the number of AF episodes in patients who do not require pacing for bradyarrhythmias. While pacing patients for the specific purpose of preventing AF is promising for some patients, further large-scale studies are needed to establish its effectiveness.

## The atrial defibrillator.

At present, two implantable cardioverter-defibrillator devices are commercially available. Larger studies and better devices in the future may make this a viable alternative.

## Surgical Maze procedure.

The surgical Maze procedure, which returns or maintains normal sinus rhythm, is indicated for those who are young, resistant to other therapies, without high surgical risk, or who need to undergo cardiac surgery for another purpose. Incisions are created in the atrial tissue to block undesired conduction paths and promote conduction in the desired manner. Using cryoablation or radiofrequency ablation to make blocks in place of the incisions shortens the operating time. In addition, using minimally invasive techniques and performing the surgery off of a bypass reduces surgical time and further limits risks. While the Maze procedure is very effective, with AF cure rates ranging from 82% to 99%, it does carry risks.<sup>8</sup>

Given the complex pathophysiology of underlying AF, it is unlikely that one therapeutic modality will adequately treat the majority of patients. Therefore, in office practice, it is important to determine what is best for the patient—a particular therapeutic protocol or a combination of them—and treat accordingly. 

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For some frequently asked questions on AF, please go to page 21.